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REPORT
117–151

NATIONAL CENTERS OF EXCELLENCE IN ADVANCED AND CONTINUOUS PHARMACEUTICAL MANUFACTURING ACT OF 2021

OCTOBER 19, 2021.—Committed to the Committee of the Whole House on the State of the Union and ordered to be printed

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Mr. PALLONE, from the Committee on Energy and Commerce, submitted the following

R E P O R T

[To accompany H.R. 4369]

The Committee on Energy and Commerce, to whom was referred the bill (H.R. 4369) to amend the 21st Century Cures Act to provide for designation of institutions of higher education that provide research, data, and leadership on continuous manufacturing as National Centers of Excellence in Continuous Pharmaceutical Manufacturing, and for other purposes, having considered the same, reports favorably thereon with amendments and recommends that the bill as amended do pass.

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The amendments are as follows:

Strike all after the enacting clause and insert the following:

SECTION 1. SHORT TITLE.

This Act may be cited as the "National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021".

SEC. 2. NATIONAL CENTERS OF EXCELLENCE IN ADVANCED AND CONTINUOUS PHARMACEUTICAL MANUFACTURING.

(a) IN GENERAL.—Section 3016 of the 21st Century Cures Act (21 U.S.C. 399h) is amended to read as follows:

"SEC. 3016. NATIONAL CENTERS OF EXCELLENCE IN ADVANCED AND CONTINUOUS PHARMACEUTICAL MANUFACTURING.

"(a) IN GENERAL.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs—

"(1) shall solicit and, beginning not later than one year after the date of enactment of the National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021, receive requests from institutions of higher education, or consortia of institutions of higher education, to be designated as a National Center of Excellence in Advanced and Continuous Pharmaceutical Manufacturing (in this section referred to as a 'National Center of Excellence') to support the advancement, development, and implementation of advanced and continuous pharmaceutical manufacturing; and

"(2) shall so designate not more than 5 institutions of higher education or consortia of such institutions that—

"(A) request such designation; and

"(B) meet the criteria specified in subsection (c).

"(b) REQUEST FOR DESIGNATION.—A request for designation under subsection (a) shall be made to the Secretary at such time, in such manner, and containing such information as the Secretary may require. Any such request shall include a description of how the institution of higher education, or consortium of institutions of higher education, meets or plans to meet each of the criteria specified in subsection (c).

"(c) CRITERIA FOR DESIGNATION DESCRIBED.—The criteria specified in this subsection with respect to an institution of higher education, or consortium of institutions of higher education, are that the institution or consortium has, as of the date of the submission of a request under subsection (a) by such institution or consortium—

"(1) physical and technical capacity for research, development, implementation, and demonstration of advanced and continuous pharmaceutical manufacturing;

"(2) manufacturing knowledge-sharing networks with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other relevant entities;

"(3) proven capacity to design, develop, implement, and demonstrate new, highly effective technologies for use in advanced and continuous pharmaceutical manufacturing;

"(4) a track record for creating, preserving, and transferring knowledge with respect to advanced and continuous pharmaceutical manufacturing;

"(5) the proven ability to facilitate training of an adequate future workforce for research on, and implementation of, advanced and continuous pharmaceutical manufacturing; and

"(6) experience in participating in and leading advanced and continuous pharmaceutical manufacturing technology partnerships with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other relevant entities—

"(A) to support companies seeking to implement advanced and continuous pharmaceutical manufacturing in the United States;

"(B) to support Federal agencies with technical assistance and employee training, which may include regulatory and quality metric guidance as applicable, and hands-on training, for advanced and continuous pharmaceutical manufacturing;

"(C) with respect to advanced and continuous pharmaceutical manufacturing, to organize and conduct research and development activities needed to create new and more effective technology, develop and share knowledge, create intellectual property, and maintain technological leadership;

"(D) to develop best practices for designing and implementing advanced and continuous pharmaceutical manufacturing processes; and

"(E) to assess and respond to the national workforce needs for advanced and continuous pharmaceutical manufacturing, including the development and implementing of training programs.

"(d) TERMINATION OF DESIGNATION.—The Secretary may terminate the designation of any National Center of Excellence designated under this section if the Secretary determines such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later than 90 days before the effective date of such a termination, the Secretary shall provide written notice to the National Center of Excellence, including the rationale for such termination.

"(e) CONDITIONS FOR DESIGNATION.—As a condition of designation as a National Center of Excellence under this section, the Secretary shall require that an institution of higher education or consortium of institutions of higher education enter into an agreement with the Secretary under which the institution or consortium agrees—

"(1) to collaborate directly with the Food and Drug Administration to publish the reports required by subsection (g);

"(2) to share data with the Food and Drug Administration regarding best practices and research generated through the funding under subsection (f);

"(3) to develop, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract research organizations or contract manufacturers that carry out drug development and manufacturing activities) and another institution or consortium designated under this section, if any, a roadmap for developing an advanced and continuous pharmaceutical manufacturing workforce;

"(4) to develop, along with industry partners and other institutions or consortia of such institutions designated under this section, a roadmap for strengthening existing, and developing new, relationships with other institutions of higher education or consortia thereof; and

"(5) to provide an annual report to the Food and Drug Administration regarding the institution's or consortium's activities under this section, including a description of how the institution or consortium continues to meet and make progress on the criteria specified in subsection (c).

"(f) FUNDING.—

"(1) IN GENERAL.—The Secretary shall award funding, through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated under this section for the purpose of studying and recommending improvements to advanced and continuous pharmaceutical manufacturing, including such improvements as may enable the Centers—

"(A) to continue to meet the conditions specified in subsection (e);

"(B) to expand capacity for research on, and development of, advanced and continuous pharmaceutical manufacturing; and

"(C) to implement research infrastructure in advanced and continuous pharmaceutical manufacturing suitable for accelerating the development of drug products needed to respond to emerging medical threats, such as emerging drug shortages, quality issues disrupting the supply chain, epidemics and pandemics, and other such situations requiring the rapid development of new products or new manufacturing processes.

"(2) CONSISTENCY WITH FDA MISSION.—As a condition on receipt of funding under this subsection, a National Center of Excellence shall agree to consider any input from the Secretary regarding the use of funding that would—

"(A) help to further the advancement of advanced and continuous pharmaceutical manufacturing through the National Center of Excellence; and

"(B) be relevant to the mission of the Food and Drug Administration.

"(3) RULE OF CONSTRUCTION.—Nothing in this section shall be construed as precluding a National Center for Excellence designated under this section from receiving funds under any other provision of this Act or any other Federal law.

"(g) ANNUAL REVIEW AND REPORTS.—

"(1) ANNUAL REPORT.—Beginning not later than one year after the date on which the first designation is made under subsection (a), and annually thereafter, the Secretary shall—

"(A) submit to Congress a report describing the activities, partnerships and collaborations, Federal policy recommendations, previous and continuing funding, and findings of, and any other applicable information from, the National Centers of Excellence designated under this section;

"(B) include in such report an accounting of the Federal administrative expenses described in subsection (i)(2) over the reporting period; and

"(C) make such report available to the public in an easily accessible electronic format on the website of the Food and Drug Administration.

"(2) REVIEW OF NATIONAL CENTERS OF EXCELLENCE AND POTENTIAL DESIGNEES.—The Secretary shall periodically review the National Centers of Excellence designated under this section to ensure that such National Centers of Excellence continue to meet the criteria for designation under this section.

"(3) REPORT ON LONG-TERM VISION OF FDA ROLE.—Not later than 2 years after the date on which the first designation is made under subsection (a), the Secretary, in consultation with the National Centers of Excellence designated under this section, shall submit a report to the Congress on the long-term vision of the Department of Health and Human Services on the role of the Food and Drug Administration in supporting advanced and continuous pharmaceutical manufacturing, including—

"(A) a national framework of principles related to the implementation and regulation of advanced and continuous pharmaceutical manufacturing;

"(B) a plan for the development of Federal regulations and guidance for how advanced and continuous pharmaceutical manufacturing can be incorporated into the development of pharmaceuticals and regulatory responsibilities of the Food and Drug Administration;

"(C) a plan for development of Federal regulations or guidance for how advanced and continuous pharmaceutical manufacturing will be reviewed by the Food and Drug Administration; and

"(D) appropriate feedback solicited from the public, which may include other institutions of higher education, large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers.

"(h) DEFINITIONS.—In this section:

"(1) ADVANCED.—The term 'advanced', with respect to pharmaceutical manufacturing, refers to an approach that incorporates novel technology, or uses an established technique or technology in a new or innovative way, that enhances drug quality or improves the performance of a manufacturing process.

"(2) CONTINUOUS.—The term 'continuous', with respect to pharmaceutical manufacturing, refers to a process—

"(A) where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and

"(B) that consists of an integrated process that consists of a series of two or more simultaneous unit operations.

"(3) INSTITUTION OF HIGHER EDUCATION.—The term 'institution of higher education' has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).

"(4) SECRETARY.—The term 'Secretary' means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.

"(i) AUTHORIZATION OF APPROPRIATIONS.—

"(1) IN GENERAL.—There is authorized to be appropriated to carry out this section $100,000,000 for the period of fiscal years 2022 through 2026.

"(2) FEDERAL ADMINISTRATIVE EXPENSES.—Of the amounts made available to carry out this section for a fiscal year, the Secretary shall not use more than eight percent for Federal administrative expenses, including training, technical assistance, reporting, and evaluation.".

(b) TRANSITION RULE.—Section 3016 of the 21st Century Cures Act (21 U.S.C. 399h), as in effect on the day before the date of the enactment of this section, shall apply with respect to grants awarded under such section before such date of enactment.

(c) CLERICAL AMENDMENT.—The item relating to section 3016 in the table of contents in section 1(b) of the 21st Century Cures Act (Public Law 114-255) is amended to read as follows:

"Sec. 3016. National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing.".

Amend the title so as to read:

A bill to amend the 21st Century Cures Act to provide for designation of institutions of higher education that provide research, data, and leadership on advanced and continuous pharmaceutical manufacturing as National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing, and for other purposes.

I. PURPOSE AND SUMMARY

H.R. 4369, the "National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021," amends the 21st Century Cures Act to provide the Food and Drug Administration (FDA) with the authority to designate institutions of higher education that provide research, data, and leadership on contin-

uous manufacturing (CM) for pharmaceuticals as National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing.

The legislation would promote the development and advancement of advanced and continuous manufacturing by directing institutions of higher education to study and recommend improvements to CM, including a roadmap for developing a workforce, collaborating, and sharing data with FDA regarding best practices and research generated, and partnering with FDA on a report to Congress regarding the role of FDA in supporting advanced and continuous manufacturing. The report would include a national framework of principles related to implementation and regulation and a plan for regulations and guidance for how advanced and continuous manufacturing can be incorporated into pharmaceutical drug development and FDA's regulatory jurisdiction.

II. Background and Need for Legislation

Conventionally, pharmaceutical drugs are made using "batch manufacturing." Batch manufacturing requires raw materials to be loaded into equipment and then undergo a sequence of lengthy steps, with quality testing of samples occurring after each step in the process.[1] Conversely, continuous manufacturing moves raw materials through a single system that incorporates monitoring and quality controls throughout the process.[2] According to FDA, which is responsible for drug development regulation, continuous manufacturing "provides a quicker, more reliable way to make pharmaceuticals."[3] This is due to quicker processing times, real-time product quality assurance, and the elimination of manual handling.[4] These advantages allow manufacturers to respond quickly to emergencies, address drug shortages, or track and discard defective products.[5] Continuous manufacturing also utilizes smaller manufacturing equipment, reducing capital and inventory costs and allowing for a reduced footprint.[6] The ability of continuous manufacturing to achieve higher yields and rely on less direct labor, compared to traditional manufacturing, can also directly impact the cost of drugs.[7]

Due to these potential benefits, the Committee has supported increased federal investment into advanced and continuous manufacturing. In the 21st Century Cures Act (P.L. 114–255), the Committee authorized a grant program through FDA to study and make recommendations for improvements to the process of continuous manufacturing of drugs and biological products, as well as

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[1] U.S. Food and Drug Administration, *Modernizing the Way Drugs Are Made: A Transition to Continuous Manufacturing* (May 17, 2017) (www.fda.gov/drugs/news-events-human-drugs/modernizing-way-drugs-are-made-transition-continuous-manufacturing).

[2] U.S. Food and Drug Administration, *Emergency Preparedness and Response, Counterterrorism and Emerging Threats, Medical Countermeasures Initiative (MCMi), MCM Issues, Advanced Manufacturing* (www.fda.gov/emergency-preparedness-and-response/mcm-issues/advanced-manufacturing).

[3] *Id.*

[4] U.S. Food and Drug Administration, *FDA Perspective on Continuous Manufacturing* (Jan. 2012) (www.fda.gov/media/85366/download).

[5] House Committee on Energy and Commerce, Testimony of Fernando J. Muzzio (Jan. 29, 2019) (docs.house.gov/meetings/IF/IF14/20200129/110423/HHRG-116-IF14-Wstate-MuzzioF-20200129.pdf).

[6] *See* note 4.

[7] *See* note 5.

similar innovative monitoring and control techniques.[8] Since enactment, eight grants have been awarded to institutions of higher education and non-profits for continuous manufacturing.[9] Yet, as of July 2020, only nine pharmaceutical drug applications had been approved by FDA using advanced manufacturing capabilities, with eight drugs relying on continuous manufacturing, and one utilizing 3D printing.[10] Additional federal support is necessary to speed the pace of adoption of advanced and continuous manufacturing.

III. COMMITTEE HEARINGS

For the purposes of section 3(c) of rule XIII of the Rules of the House of Representatives, the following hearing was used to develop or consider H.R. 4369:

The Subcommittee on Health held a legislative hearing in the 116th Congress on January 29, 2020, entitled "Improving Safety and Transparency in America's Food and Drugs." The Subcommittee received testimony from the following witnesses:

Panel I

- Jeff Allen, Ph.D., President and CEO, Friends of Cancer Research;
- Richard Kaeser, Vice President, Global Brand Protection, Johnson & Johnson;
- Fernando Muzzio, Ph.D., Distinguished Professor, Chemical and Biochemical Engineering, Rutgers, the State University of New Jersey; and
- Kao-Ping Chua, M.D., Ph.D., Assistant Professor, Department of Pediatrics University of Michigan Medical School.

Panel II

- Melanie Benesh, Legislative Attorney, Environmental Working Group;
- Tom Balmer, Executive Vice President, National Milk Producers Federation;
- J. David Carlin, Senior Vice President of Legislative Affairs and Economic Policy, International Dairy Foods Association;
- Douglas Corey, D.V.M., Past President, American Association of Equine Practitioners;
- Talia Day, Patient Advocate;
- Paul C. DeLeo, Ph.D., Principal, Integral Consulting, Inc.;
- Mardi Mountford, President, Infant Nutrition Council of America;
- Nancy Perry, Senior Vice President, Government Relations, American Society for the Prevention of Cruelty to Animals; and
- Sara Sorscher, Deputy Director of Regulatory Affairs, Center for Science in the Public Interest.

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[8] Pub. L. No. 114–255, Sec. 3016 (2016) (www.congress.gov/114/plaws/publ255/PLAW-114publ255.pdf).

[9] *See* note 2.

[10] Email from Staff, U.S. Food and Drug Administration, to Majority Staff, House Committee on Energy and Commerce (July 27, 2020).

IV. COMMITTEE CONSIDERATION

Chairman Frank Pallone, Jr. (D–NJ) and Representative Brett Guthrie (R–KY) introduced H.R. 4369, the "National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021," on July 6, 2021, which was referred to the Committee on Energy and Commerce. Subsequently, on July 7, 2021, H.R. 4369 was referred to the Subcommittee on Health.

On July 15, 2021, the Subcommittee on Health met in a hybrid open markup session, pursuant to notice, to consider H.R. 4369. During consideration of the bill, an amendment in the nature of a substitute (AINS) offered by Chairman Pallone was agreed to by a voice vote. Upon conclusion of consideration of the bill, the Subcommittee ordered H.R. 4369 reported favorably to the full Committee, amended, by a voice vote.

On July 21, 2021, the full Committee met in open markup session, pursuant to notice, to consider H.R. 4369 and 23 other bills. During consideration of the bill, an amendment offered by Chairman Pallone was agreed to by a voice vote. Upon conclusion of consideration of the bill, the full Committee agreed to a motion on final passage offered by Chairman Pallone to order H.R. 4369 reported favorably to the House, amended, by a voice vote.

V. COMMITTEE VOTES

Clause 3(b) of rule XIII of the Rules of the House of Representatives requires the Committee to list each record vote on the motion to report legislation and amendments thereto. The Committee advises that there were no record votes taken on H.R. 4369, including a motion by Mr. Pallone ordering H.R. 4369 favorably reported to the House, amended.

VI. OVERSIGHT FINDINGS

Pursuant to clause 3(c)(1) of rule XIII and clause 2(b)(1) of rule X of the Rules of the House of Representatives, the oversight findings and recommendations of the Committee are reflected in the descriptive portion of the report.

VII. NEW BUDGET AUTHORITY, ENTITLEMENT AUTHORITY, AND TAX EXPENDITURES

Pursuant to 3(c)(2) of rule XIII of the Rules of the House of Representatives, the Committee adopts as its own the estimate of new budget authority, entitlement authority, or tax expenditures or revenues contained in the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

The Committee has requested but not received from the Director of the Congressional Budget Office a statement as to whether this bill contains any new budget authority, spending authority, credit authority, or an increase or decrease in revenues or tax expenditures.

VIII. Federal Mandates Statement

The Committee adopts as its own the estimate of Federal mandates prepared by the Director of the Congressional Budget Office pursuant to section 423 of the Unfunded Mandates Reform Act.

IX. Statement of General Performance Goals and Objectives

Pursuant to clause 3(c)(4) of rule XIII, the general performance goal or objective of this legislation is to support the advancement and development of continuous manufacturing through the designation of institutions of higher education as National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing, which will provide research, data, and leadership on advanced and continuous manufacturing.

X. Duplication of Federal Programs

Pursuant to clause 3(c)(5) of rule XIII, no provision of H.R. 4369 is known to be duplicative of another Federal program, including any program that was included in a report to Congress pursuant to section 21 of Public Law 111–139 or the most recent Catalog of Federal Domestic Assistance.

XI. Committee Cost Estimate

Pursuant to clause 3(d)(1) of rule XIII, the Committee adopts as its own the cost estimate prepared by the Director of the Congressional Budget Office pursuant to section 402 of the Congressional Budget Act of 1974.

XII. Earmarks, Limited Tax Benefits, and Limited Tariff Benefits

Pursuant to clause 9(e), 9(f), and 9(g) of rule XXI, the Committee finds that H.R. 4369 contains no earmarks, limited tax benefits, or limited tariff benefits.

XIII. Advisory Committee Statement

No advisory committee within the meaning of section 5(b) of the Federal Advisory Committee Act was created by this legislation.

XIV. Applicability to Legislative Branch

The Committee finds that the legislation does not relate to the terms and conditions of employment or access to public services or accommodations within the meaning of section 102(b)(3) of the Congressional Accountability Act.

XV. Section-by-Section Analysis of the Legislation

Section 1. Short title

Section 1 designates that the short title may be cited as the "National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021."

Sec. 2. National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing

Section 2 amends section 3016 of the 21st Century Cures Act to establish the National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing program. Subsection (a) of the amended section 3016 requires within one year of enactment that the Secretary of HHS, acting through the Commissioner of Food and Drugs, solicit and receive requests from institutions of higher education, or consortia of institutions of higher education, to be designated as a National Center of Excellence in Advanced and Continuous Pharmaceutical Manufacturing (referred to as a 'National Center of Excellence') to support the advancement, development, and implementation of advanced manufacturing and CM. FDA shall designate not more than five institutions of higher education or consortia that request such designation and meets the criteria identified.

Subsection (b) of the amended section 3016 requires designation requests to be made at such time, in such manner, and containing such information as FDA may require. Any request shall include a description of how the institution of higher education meets or plans to meet each of the criteria identified.

Subsection (c) of the amended section 3016 describes the criteria that an institution of higher education should have at the date of submission of a designation request. This shall include: (1) physical and technical capacity for research, development, implementation, and demonstration of advanced and continuous manufacturing; (2) manufacturing knowledge-sharing networks with other institutions of higher education, manufacturers (large, small, generic, nonprescription, and contract), and other relevant entities; (3) proven capacity to design and demonstrate new, highly effective technology for use in advanced and continuous manufacturing; (4) a track record for creating, preserving, and transferring knowledge with respect to advanced and continuous manufacturing; (5) the proven ability to facilitate training of a future workforce for research on and implementation of advanced and continuous manufacturing; (6) experience participating in and leading advanced and continuous manufacturing technology partnerships with other institutions of higher education, manufacturers (large, small, generic, nonprescription, and contract), and other relevant entities to support companies with implementation of advanced and continuous manufacturing in the United States; (7) to support federal agencies with technical assistance, which may include regulatory and quality metric guidance, as applicable, and hands-on training for advanced and continuous manufacturing; (8) to organize and conduct research and development activities needed to create new and more effective technology, develop and share knowledge, create intellectual property, and maintain technology leadership; (9) to develop best practices for designing and implementing advanced and continuous manufacturing processes; and (10) to assess and respond to the national workforce needs for advanced and continuous manufacturing, including the development of training programs.

Subsection (d) of the amended section 3016 grants FDA the authority to terminate the designation of any National Center of Excellence if it is determined that such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later

than 90 days before the effective date of such termination, FDA shall provide written notice to the institution and a rationale for such termination.

Subsection (e) of the amended section 3016 specifies that as a condition of designation, FDA shall require that an institution of higher education, or consortium of institutions, enter into an agreement under which the institution agrees to: collaborate with FDA to publish the reports required under subsection (g); share data with FDA regarding best practices and research generated through funding under subsection (f); develop a roadmap, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers) and other designated institutions for developing an advanced and continuous manufacturing workforce; develop, along with industry partners and other designated institutions, a roadmap for strengthening existing and new relationships with other institutions or consortia of institutions; and to provide an annual report to FDA regarding the institution's or consortium's activities, including how the institution or consortium continues to meet and make progress on the criteria listed in subsection (c).

Subsection (f) of the amended section 3016 requires FDA to award funding through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated for the purpose of studying and recommending improvements to advanced and continuous manufacturing, including such improvements as may enable the Centers to continue to meet the conditions specified in subsection (e); to expand capacity for research on, and development of, advanced and continuous manufacturing; and to implement research infrastructure in advanced and continuous manufacturing suitable for accelerating the development of drug products needed to respond to emerging medical threats, such as emerging drug shortages, quality issues disrupting the supply chain, epidemics and pandemics, and other such situations requiring the rapid development of new products or new manufacturing processes. As a condition of receipt of funding, a designated institution shall agree to consider any input from FDA to ensure such funding helps further the advancement of advanced and continuous manufacturing through the National Center of Excellence and is relevant to the mission of FDA. A rule of construction ensures that no element of the amended section 3016 shall be construed as restricting a National Center of Excellence from receiving funding under another section of the 21st Century Cures Act or any other federal law.

Subsection (g) of the amended section 3016 requires that not later than one year after the first designation of a National Center of Excellence, FDA shall submit to Congress an annual report describing the activities, partnerships, collaborations, federal policy recommendations, previous and continued funding, and findings of, and any other applicable information, from the designated National Centers of Excellence. The report shall also include an accounting of Federal administrative expenses incurred. Such report shall be made publicly available on the website of the FDA. FDA is also required to periodically review designated National Centers of Excellence to ensure that such Centers continue to meet the criteria for designation. Within two years of the first designation, the Sec-

retary of HHS, in consultation with the National Centers of Excellence, shall submit to Congress a report on the long-term vision of HHS on the role of the FDA in supporting advanced and continuous manufacturing, including a national framework of principles related to the implementation and regulation of advanced and continuous manufacturing, a plan for the development of federal regulations and guidance for how advanced and continuous manufacturing can be incorporated into the development of drugs and regulatory responsibilities of FDA, and appropriate feedback solicited from the public, which may include other institutions and manufacturers (large, small, generic, nonprescription, and contract).

Subsection (h) of the amended section 3016 defines relevant terms in H.R. 4369 including "advanced manufacturing," "continuous manufacturing," "institution of higher education," and "Secretary." As defined in H.R. 4369, the term "advanced manufacturing" means an approach for the manufacturing of pharmaceuticals that incorporates novel technology, or uses an established technique or technology in a new or innovative way that enhances drug quality or improves the manufacturing process. The term "continuous manufacturing," as defined in H.R. 4369, means a process where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and consists of an integrated process of a series of two or more unit operations. The term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)). The term "Secretary," as defined in H.R. 4369, means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.

Subsection (i) authorizes $100 million for the period of FY 2022 through 2026 to be appropriated to carry out the activities described in the section, not more than eight percent of which can be used for Federal administrative expenses, including training, technical assistance, reporting, and evaluation.

Section 2 also clarifies that section 3016 of the 21st Century Cures Act, as in effect on the day before the date of the enactment of this section, shall apply with respect to grants awarded under this section before such date of enactment, and includes a clerical amendment to alter the Table of Contents in the 21st Century Cures Act.

XVI. Changes in Existing Law Made by the Bill, as Reported

In compliance with clause 3(e) of rule XIII of the Rules of the House of Representatives, changes in existing law made by the bill, as reported, are shown as follows (existing law proposed to be omitted is enclosed in black brackets, new matter is printed in italics, and existing law in which no change is proposed is shown in roman):

21ST CENTURY CURES ACT

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SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

(b) TABLE OF CONTENTS.—The table of contents for this Act is as follows:

DIVISION A—21ST CENTURY CURES

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TITLE III—DEVELOPMENT

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Subtitle B—Advancing New Drug Therapies

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[SEC. 3016. GRANTS FOR STUDYING CONTINUOUS DRUG MANUFACTURING.

[(a) IN GENERAL.—The Secretary of Health and Human Services may award grants to institutions of higher education and nonprofit organizations for the purpose of studying and recommending improvements to the process of continuous manufacturing of drugs and biological products and similar innovative monitoring and control techniques.

[(b) DEFINITIONS.—In this section—

[(1) the term "drug" has the meaning given such term in section 201 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321);

[(2) the term "biological product" has the meaning given such term in section 351(i) of the Public Health Service Act (42 U.S.C. 262(i)); and

[(3) the term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).]

SEC. 3016. NATIONAL CENTERS OF EXCELLENCE IN ADVANCED AND CONTINUOUS PHARMACEUTICAL MANUFACTURING.

(a) IN GENERAL.—The Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs—

(1) shall solicit and, beginning not later than one year after the date of enactment of the National Centers of Excellence in Advanced and Continuous Pharmaceutical Manufacturing Act of 2021, receive requests from institutions of higher education, or consortia of institutions of higher education, to be designated as a National Center of Excellence in Advanced and Continuous Pharmaceutical Manufacturing (in this section referred to as a "National Center of Excellence") to support the advancement, development, and implementation of advanced and continuous pharmaceutical manufacturing; and

(2) shall so designate not more than 5 institutions of higher education or consortia of such institutions that—

(A) request such designation; and

(B) meet the criteria specified in subsection (c).

(b) REQUEST FOR DESIGNATION.—A request for designation under subsection (a) shall be made to the Secretary at such time, in such manner, and containing such information as the Secretary may require. Any such request shall include a description of how the institution of higher education, or consortium of institutions of higher education, meets or plans to meet each of the criteria specified in subsection (c).

(c) CRITERIA FOR DESIGNATION DESCRIBED.—The criteria specified in this subsection with respect to an institution of higher education, or consortium of institutions of higher education, are that the institution or consortium has, as of the date of the submission of a request under subsection (a) by such institution or consortium—

(1) physical and technical capacity for research, development, implementation, and demonstration of advanced and continuous pharmaceutical manufacturing;

(2) manufacturing knowledge-sharing networks with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other relevant entities;

(3) proven capacity to design, develop, implement, and demonstrate new, highly effective technologies for use in advanced and continuous pharmaceutical manufacturing;

(4) a track record for creating, preserving, and transferring knowledge with respect to advanced and continuous pharmaceutical manufacturing;

(5) the proven ability to facilitate training of an adequate future workforce for research on, and implementation of, advanced and continuous pharmaceutical manufacturing; and

(6) experience in participating in and leading advanced and continuous pharmaceutical manufacturing technology partnerships with other institutions of higher education, large and small pharmaceutical manufacturers, generic and nonprescription manufacturers, contract manufacturers, and other relevant entities—

(A) to support companies seeking to implement advanced and continuous pharmaceutical manufacturing in the United States;

(B) to support Federal agencies with technical assistance and employee training, which may include regulatory and quality metric guidance as applicable, and hands-on train-

ing, for advanced and continuous pharmaceutical manufacturing;

(C) with respect to advanced and continuous pharmaceutical manufacturing, to organize and conduct research and development activities needed to create new and more effective technology, develop and share knowledge, create intellectual property, and maintain technological leadership;

(D) to develop best practices for designing and implementing advanced and continuous pharmaceutical manufacturing processes; and

(E) to assess and respond to the national workforce needs for advanced and continuous pharmaceutical manufacturing, including the development and implementing of training programs.

(d) TERMINATION OF DESIGNATION.—The Secretary may terminate the designation of any National Center of Excellence designated under this section if the Secretary determines such National Center of Excellence no longer meets the criteria specified in subsection (c). Not later than 90 days before the effective date of such a termination, the Secretary shall provide written notice to the National Center of Excellence, including the rationale for such termination.

(e) CONDITIONS FOR DESIGNATION.—As a condition of designation as a National Center of Excellence under this section, the Secretary shall require that an institution of higher education or consortium of institutions of higher education enter into an agreement with the Secretary under which the institution or consortium agrees—

(1) to collaborate directly with the Food and Drug Administration to publish the reports required by subsection (g);

(2) to share data with the Food and Drug Administration regarding best practices and research generated through the funding under subsection (f);

(3) to develop, along with industry partners (which may include large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract research organizations or contract manufacturers that carry out drug development and manufacturing activities) and another institution or consortium designated under this section, if any, a roadmap for developing an advanced and continuous pharmaceutical manufacturing workforce;

(4) to develop, along with industry partners and other institutions or consortia of such institutions designated under this section, a roadmap for strengthening existing, and developing new, relationships with other institutions of higher education or consortia thereof; and

(5) to provide an annual report to the Food and Drug Administration regarding the institution's or consortium's activities under this section, including a description of how the institution or consortium continues to meet and make progress on the criteria specified in subsection (c).

(f) FUNDING.—

(1) IN GENERAL.—The Secretary shall award funding, through grants, contracts, or cooperative agreements, to the National Centers of Excellence designated under this section for the purpose of studying and recommending improvements to

advanced and continuous pharmaceutical manufacturing, including such improvements as may enable the Centers—

(A) to continue to meet the conditions specified in subsection (e);

(B) to expand capacity for research on, and development of, advanced and continuous pharmaceutical manufacturing; and

(C) to implement research infrastructure in advanced and continuous pharmaceutical manufacturing suitable for accelerating the development of drug products needed to respond to emerging medical threats, such as emerging drug shortages, quality issues disrupting the supply chain, epidemics and pandemics, and other such situations requiring the rapid development of new products or new manufacturing processes.

(2) CONSISTENCY WITH FDA MISSION.—As a condition on receipt of funding under this subsection, a National Center of Excellence shall agree to consider any input from the Secretary regarding the use of funding that would—

(A) help to further the advancement of advanced and continuous pharmaceutical manufacturing through the National Center of Excellence; and

(B) be relevant to the mission of the Food and Drug Administration.

(3) RULE OF CONSTRUCTION.—Nothing in this section shall be construed as precluding a National Center for Excellence designated under this section from receiving funds under any other provision of this Act or any other Federal law.

(g) ANNUAL REVIEW AND REPORTS.—

(1) ANNUAL REPORT.—Beginning not later than one year after the date on which the first designation is made under subsection (a), and annually thereafter, the Secretary shall—

(A) submit to Congress a report describing the activities, partnerships and collaborations, Federal policy recommendations, previous and continuing funding, and findings of, and any other applicable information from, the National Centers of Excellence designated under this section;

(B) include in such report an accounting of the Federal administrative expenses described in subsection (i)(2) over the reporting period; and

(C) make such report available to the public in an easily accessible electronic format on the website of the Food and Drug Administration.

(2) REVIEW OF NATIONAL CENTERS OF EXCELLENCE AND POTENTIAL DESIGNEES.—The Secretary shall periodically review the National Centers of Excellence designated under this section to ensure that such National Centers of Excellence continue to meet the criteria for designation under this section.

(3) REPORT ON LONG-TERM VISION OF FDA ROLE.—Not later than 2 years after the date on which the first designation is made under subsection (a), the Secretary, in consultation with the National Centers of Excellence designated under this section, shall submit a report to the Congress on the long-term vision of the Department of Health and Human Services on the role of the Food and Drug Administration in supporting ad-

vanced and continuous pharmaceutical manufacturing, including—

(A) a national framework of principles related to the implementation and regulation of advanced and continuous pharmaceutical manufacturing;

(B) a plan for the development of Federal regulations and guidance for how advanced and continuous pharmaceutical manufacturing can be incorporated into the development of pharmaceuticals and regulatory responsibilities of the Food and Drug Administration;

(C) a plan for development of Federal regulations or guidance for how advanced and continuous pharmaceutical manufacturing will be reviewed by the Food and Drug Administration; and

(D) appropriate feedback solicited from the public, which may include other institutions of higher education, large and small biopharmaceutical manufacturers, generic and nonprescription manufacturers, and contract manufacturers.

(h) DEFINITIONS.—In this section:

(1) ADVANCED.—The term "advanced", with respect to pharmaceutical manufacturing, refers to an approach that incorporates novel technology, or uses an established technique or technology in a new or innovative way, that enhances drug quality or improves the performance of a manufacturing process.

(2) CONTINUOUS.—The term "continuous", with respect to pharmaceutical manufacturing, refers to a process—

(A) where the input materials are continuously fed into and transformed within the process, and the processed output materials are continuously removed from the system; and

(B) that consists of an integrated process that consists of a series of two or more simultaneous unit operations.

(3) INSTITUTION OF HIGHER EDUCATION.—The term "institution of higher education" has the meaning given such term in section 101(a) of the Higher Education Act of 1965 (20 U.S.C. 1001(a)).

(4) SECRETARY.—The term "Secretary" means the Secretary of Health and Human Services, acting through the Commissioner of Food and Drugs.

(i) AUTHORIZATION OF APPROPRIATIONS.—

(1) IN GENERAL.—There is authorized to be appropriated to carry out this section $100,000,000 for the period of fiscal years 2022 through 2026.

(2) FEDERAL ADMINISTRATIVE EXPENSES.—Of the amounts made available to carry out this section for a fiscal year, the Secretary shall not use more than eight percent for Federal administrative expenses, including training, technical assistance, reporting, and evaluation.

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